REMARKS/ARGUMENTS

Applicants acknowledge, with thanks, the Office Action mailed August 1, 2007. This amendment and response is responsive to that Office Action. Claims 1-4, 6, 7, 9-15, 20-23, 30, 34-36, and 41-43 are pending in the subject application and stand rejected. Accordingly, independent claims 1, 30, and 34 have been amended. Dependent claims 2, 4, 6, 9-13, 20-23, 35, and 36 have been amended, with claims 20, 21, and 23 being rewritten in independent form in accordance with the Examiner's comments in the aforementioned Office Action. New independent claims 20, 21, and 23 have been amended to include all the limitations of the base claim and any intervening claims, thus no new matter has been added. Thus, claims 20, 21, and 23 include each and every limitation of claim 1 and any intervening claims. Claim 7 has been canceled.

NON-ART MATTERS

I. Rejection of claims 1-4, 6, 7, 9-15, 20-23, 30, 34-36, and 41-43 under 35 U.S.C. § 112, First Paragraph

Claims 1-4, 6, 7, 9-15, 20-23, 30, 34-36, and 41-43 have been rejected under the first paragraph of 35 U.S.C. § 112 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time of filing, had possession of the claimed invention. That is, the Examiner notes that while the specification is enabling for methods of preparing a reprogrammed diploid mammalian cell, the specification is not enabling for preparing a reprogrammed diploid mammalian cell from non-mammalian cells or non-mammalian nuclei. By this amendment, all relevant claims, including all independent claims, have been amended to clarify that the donor cell or donor nucleus and the recipient cell be mammalian. Thus, all occurrences of such terms in the claims have been prefaced with the mammalian limitation. Reconsideration is thus respectfully requested.

With respect to previously presented independent claims 1, 30, and 34, and new independent claims 20, 21, and 23, Applicants note that the Examiner has repeated the rejection of the aforementioned claims under the first paragraph of 35 U.S.C. § 112 regarding the means to determine the recipient and donor nuclei as claimed. That is, according to the outstanding Office Action, the Examiner opines that the specification describes only a single method, e.g., piezo-

impact microinjection system of Wakayama (1998). Applicants respectfully traverse the rejection. For example, page 6, paragraph 1 of the instant specification states that the transfer of the donor cell or donor nucleus to the recipient cell can be carried out in many different ways, e.g. microsurgical injection, cell fusion including electrofusion, chemical reagents such as polyethyleneglycol, inactivated viruses such as the Sendai virus, and the like. Similarly, the recipient nucleus or nuclear material may be removed or destroyed by exploiting the recipient cell's developmental self-correction mechanisms (page 8, lines 14-17) or by removing the recipient nucleus through an incision site in the recipient cell (page 9, lines 9-11). Furthermore, Applicants respectfully submit that the subject specification also provides descriptions of numerous methods for visualizing the donor and recipient nuclei to facilitate such manipulations and assess whether the recipient nucleus has been removed are available to those skilled in the art, e.g. the visualization techniques on page 8, lines 18-22. Thus, Applicants respectfully submit that in light of these passages in the specification, the person of ordinary skill in the art would readily be able to carry out the methods of claims 1, 20, 21, 23, 30, and 34 and withdrawal of this ground of rejection is requested.

The Examiner has also maintained the rejection under the first paragraph of 35 U.S.C. § 112 regarding the reproducibility of the methods for producing mammals, mammalian organs or mammalian tissues set forth in the pending claims. The Applicants note that the Examiner's objections appear to focus, in particular, on a statement in Pennisi and Vogel, which states that even pregnancy does not assure term delivery of a cloned mammal. Applicants respectfully submit that the instant specification, with respect to such enablement concerns, provides adequate examples of successful experiments regarding the methodology of the rejected claims, i.e. independent claims 1, 20, 21, 23, 30, and 34.

The Applicants respectfully assert that the concerns expressed by the Examiner with respect to Pennisi and Vogel are not relevant to the production of mammalian tissues or organs. Applicants note that the outstanding Office Action indicates the Examiner's acceptance that the present claims are enabled for the production of reprogrammed mammalian cells and submit that it would have been well within the capabilities of the skilled artisan to use such reprogrammed cells to produce tissues or organs. For example, such tissues or organs could be generated from cells isolated from mammalian embryos prepared according to the invention of claims 1, 20, 21,

23, 30, and 34 without the need for a full term pregnancy or even implantation of such embryos. Applicants acknowledge, with thanks, the Examiner's confirmation that the claimed methods of the subject application can be used for the production of mammalian embryos, "...applicant has provided evidence that their method produces a greater number of blastocysts using pig donor cells and oocytes". Page 4, first paragraph of the Office Action.

Given this superior performance of the method embodied in claims 1, 20, 21, 23, 30, and 34 of the subject application, Applicants submit that there is no rationale to doubt the use of the said claimed method in the generation of mammals. In this regard, Applicants note that Pennisi and Vogel report:

> PPL spent more than a year trying to clone pigs with the techniques the company and Wilmut had used for sheep [i.e. a nuclear transfer method]. Each attempt failed. Pig embryos proved too fragile, and the cells often broke apart during nuclear transfer or handling. In those rare instances when the researchers were able to add the donor nucleus to the egg and then activate development, the embryos never made it to the blastocyst stage.

In contrast to the failure of nuclear transfer methods to provide pig blastocysts reported by Pennisi and Vogel, the nuclear addition methods of the present invention have been demonstrated to provide pig blastocysts (see Examples 3-6). Thus, Applicants respectfully submit that a person of ordinary skill in the art would be able to generate mammals using the method embodied in the claims and described in the specification, not only in animals considered refractory to nuclear manipulation methods (e.g. pigs), but also in mammals considered to be more amenable to such techniques (e.g. the mice described in Example 2 of the instant specification). Thus, given the disclosure in the present specification, the skilled artisan would have a reasonable expectation of success (i.e. the production of at least some live-born mammals).

The Applicants thereby submit that the skilled artisan can successfully carry out the method of claims 1, 20, 21, 23, 30, and 34 based on the teachings of the instant specification as filed and in doing so, can expect, as substantiated by the specification, to obtain greater success than using previously known methods. Thus, Applicants submit that neither the efficiency of the method of claims 1, 20, 21, 23, 30, and 34, nor the explanation as to why nuclear addition, as

opposed to nuclear transfer, provides improved results, are relevant to the question of enablement.

Claims 2-4, 6, 9-15, 22, 35-36, and 41-43 depend directly from claims 1, 20, 21, 23, 30, and 34 and as such include each and every limitation of the base claims. For the reasons set forth above with respect to their independent base claims 1, 20, 21, 23, 30, and 34, Applicants respectfully submit that claims 2-4, 6, 9-15, 22, 35-36, and 41-43 are also fully enabled in accordance with the provisions of the first paragraph of 35 U.S.C. § 112 and request withdrawal of this rejection.

II. Rejection of claims 1, 7, 9, 20-23, and 30 under 35 U.S.C. § 112, Second Paragraph

Claims 1, 7, 9, 20-23, and 30 have been rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

The Office Action received from the Examiner does not indicate the rationale for the rejection of claim 1 under the second paragraph of 35 U.S.C. § 112 and Applicants assume that such rejection of claim 1 was satisfactorily addressed in Applicants' response to the previous Office Action as indicated in the withdrawal of the rejection in the instant Office Action.

Applicants have canceled claim 7 and thus respectfully request withdrawal of this rejection.

With respect to claim 9, Applicants respectfully submit that claim 9 does add a further limitation to claim 1. Claim 1, as currently amended, designates the donor cell or donor nucleus as a somatic cell or a somatic cell nucleus. Claim 9 designates the donor cell or donor cell nucleus as a somatic stem cell or a nucleus derived therefrom. Applicants submit that not all somatic cells are somatic stem cells and thus claim 9 does add a further limitation to claim 1. Reconsideration and withdrawal of this rejection is thus respectfully requested.

Applicants have amended claims 20-23 in accordance with the Examiner's suggestions, making claims 20, 21 and 23 independent. Each of the newly independent claims include all the limitations of claim 1. Applicants respectfully submit that the wording of these independent claims clearly indicate extensions of claim 1, in which additional steps are carried out. Thus,

Applicants argue that the methods of generating a cell line, tissue, organ or mammalian embryo as embodied in claims 20, 21 and 23 correspond to the reprogramming of claim 1, as expressed in the currently amended claims. That is, the subject matter of claims 20, 21 and 23 relates to the same goal and the same inventive concept as that of claim 1, i.e. the provision of cells, cell lines, and the like for agricultural, medical, veterinary and research applications through the provision of a reprogrammed diploid mammalian cell. Claim 22 depends from claim 20 and includes all the limitations thereof, thus no longer dependent upon claim 1.

Claim 30 has been amended in accordance with the Examiner's suggestion. Accordingly, Applicants respectfully request withdrawal and reconsideration of the rejection of claim 30.

CONCLUSION

For the reasons set forth above, Applicants respectfully request the withdrawal of the rejections. The Examiner is invited to contact the undersigned if there are any other matters to be discussed to advance the prosecution of this application.

If there are any fees necessitated by the foregoing communication, the Commissioner is hereby authorized to charge such fees to our Deposit Account No. 50-0902, referencing our Docket No. 78870/00004.

Respectfully submitted,

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